EPILEPSY

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Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "EPILEPSY Newsletter" which contains latest and interesting news in the field of Neuropsychiatry.

This issue contains:

1. Clinical outcomes in 47 cases of transitory epileptic amnesia during a 10-year follow-up cohort study
2. A 2-year follow-up on the use of magnetoencephalography combined with stereo-electroencephalography in resective epilepsy surgery
3. For the treatment of drug-resistant epilepsy in children, stereotactic laser interstitial thermal therapy corpus callosotomy was used.
4. A case report of successful medical therapy of West syndrome with a KCNA2 mutation.

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Clinical outcomes in 47 cases of transitory epileptic amnesia during a 10-year follow-up cohort study

Transient epileptic amnesia (TEA) is an unrecognized form of late-onset temporal lobe epilepsy that manifests as ictal episodes of transient amnesia, either retrograde or anterograde, of variable length. It usually occurs between the ages of 50 and 70. The episodes are usually brief (less than one hour), but they might linger for hours, mimicking benign transitory global amnesia (TGA).[1] The most common treatment for TEA is a low-dose antiseizure drug, which has a high percentage of seizure cessation. Although this addresses the ictal memory disturbance, many group studies comparing patients on treatment with matched healthy controls suggest long-term cognitive consequences such as patchy retrograde amnesia for significant life events, accelerated forgetting of recently acquired memories, and topographical memory impairment. The aim of this study was to learn more about TEA's long-term prognosis in terms of seizure control, memory, medical comorbidities, and life expectancy.[2]

For 47 persons diagnosed with TEA who had enrolled in the Impairment of Memory in Epilepsy (TIME) study ten years ago, current clinical information was gathered. Information about comorbid conditions was rigorously obtained at the start of the trial. The family doctor was contacted for information on later diagnoses, seizure activity, medication changes, and reports of cognitive impairment. The variables of interest were compared to population statistics from the United Kingdom.

The cohort's mortality rate was 45 percent, with an average age at death of 82.5 years. For the most part, seizures were successfully managed, but several drugs required dose and type modifications (28 percent). A limited number of people (three in all) were able to go without medication and remain seizure-free. Cardiovascular problems were common (78.7%), with hypertension being the most common (55.3 percent). Autoimmune disorders (25.5%), cancer (23.4%), and depression (21.3%) were also often mentioned. Despite the fact that persistent memory issues were common, dementia was diagnosed in seven cases (14.9 percent). In TEA, life expectancy and comorbidities were comparable to population averages. (Table 1)

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Table 1 : Comparison of prevalence of common conditions in TEA cohort vs UK-wide values

	TEA (%)		Health Survey for England (%)			
Condition	**<75**	**75+**	**65-74**	**75+**		
IHD	16.7	22.9	11.0 (p = 0.53)	16.0 (p = 0.28)		
Stroke	8.3	8.6	5.0 (p = 0.60)	9.0 (p=0.94)		
Hypertension	58.3	54.3	58.7 (p = 0.98)	61.6 (p=0.41)		
			UK general practice 2000 -2016 (%)			
		65-74	**75-84**	**85+**		
AF	8.5	6	14	22		
			Dementia UK report (%)			
		65-69	**70-74**	**80-84**	**85-89**	**75-79**
Dementia	14.9	1.7	3	11.1	18.3	6
			Office for National lifetime prevalence (%)			
Depression		21.3	19.7			

The current study is the first to present long-term follow-up data in a large group of TEA patients, including information on broad clinical outcomes (mortality, comorbidities, including dementia risk), as well as how this type of epilepsy behaves over a 10-year period (regarding seizures and medication).[2] Persistent memory issues or decrease in some aspects of memory that were not severe enough to warrant a dementia diagnosis were widespread among the subject. This is in line with the well-documented high prevalence of memory problems reported at the time of TEA diagnosis. Although it is encouraging that the proportion of people diagnosed with dementia has not increased in comparison to the general population, and previous research has shown stable cognitive function over a 20-year period of follow-up, given that the majority of people still have memory problems, there is a clear need for future research to focus on establishing a cause. Approximately one-fifth of the group had a history of mood problems throughout their lives. This was most typically manifested as significant depression, which occurred in half of the cases prior to the commencement of TEA. In several cases (two), the onset of depression coincided with the commencement of TEA. Enhanced anxiety was also recognised as a feature during seizures in three patients, however it did not qualify for a formal diagnosis. Although our findings are similar to the 19.7% lifetime prevalence of depression in adults reported in the UK.[3,2]

Overall, the current study's findings indicate that TEA does not appear to shorten life expectancy or raise the risk of dementia. However, it's a good idea to get the medication reviewed on a regular basis to confirm that it's still working and to help manage any lingering memory or mood issues.

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A 2-year follow-up on the use of magnetoencephalography combined with stereo-electroencephalography in resective epilepsy surgery

Epilepsy is a brain disorder marked by an enduring proclivity for epileptic seizures as well as the neurobiological, cognitive, psychological, and social repercussions of this condition. It is responsible for 0.5 percent of the global illness burden.[1] Anti-seizure medication resistance affects about 30% of all epilepsy patients, resulting in severe morbidity and mortality. Invasive electroencephalographic techniques, such as stereo-electroencephalography (SEEG), are the gold standard in seizure-focus localization, but they are limited by factors such as limited coverage per electrode, higher surgical risk due to the higher number of electrodes implanted, and high cost.[2] To this goal, magnetoencephalography (MEG) has been found to yield clinically useful information. However, it is still underutilised, and in the vast majority of medical centres, it is not part of the standard of treatment.[3] The aim of this study was to assess how accurate MEG was at determining the seizure onset zone (SOZ).

The study looked at 140 patients who had SEEG implantation. Presurgical MEG examination and proper post-surgical follow-up were provided to 42 patients. The dipole clusters were used to build the SEEG plan, and the resections were carried out based on the SEEG recordings (Figure 1). The association between the pattern of MEG dipole clusters and SEEG sampling and the final resective surgical prognosis was studied.

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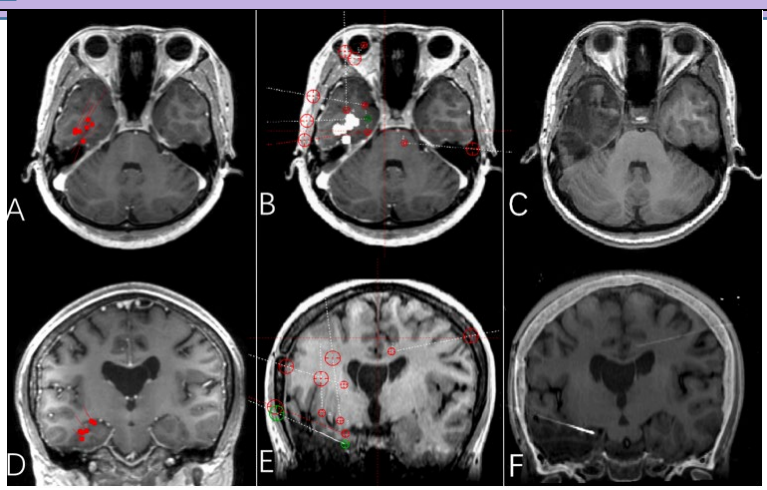

Figure 1: MEG navigate SEEG implanting and postsurgical follow-up review

The study comprised 42 individuals who had at least a two-year postoperative follow-up (mean 34.1 months) (Figure 2). Patients with concordant localization between MEG and SEEG examination had a greater chance of seizure-free outcomes (p=0.046, $\chi 2$ =4.835, odds ratio=5.00, 95 percent CI=1.12-22.30). Complete SEEG electrode sampling of MEG dipole clusters were detected in 23 (54%) patients, who had a better chance of seizure-free outcomes than those who had incomplete sampling (p<0.001, odds ratio=16.67, 95 percent CI=3.11-89.28). After resective surgery, MEG data demonstrating a single, tight cluster or stable orientation were linked to better seizure outcomes.

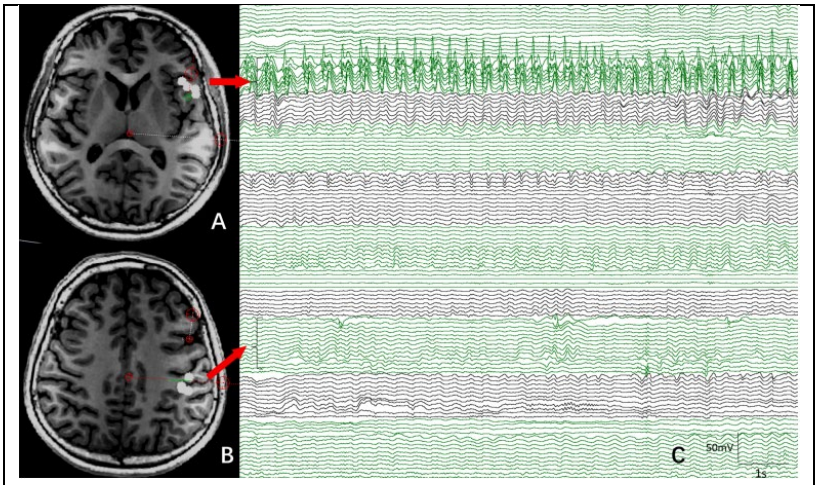

Figure 2: A & B- The result of MEG and the planned SEEG electrode pathway which would completely sample all MEG clusters. Fig C shows the ictal SEEG monitoring data.

This study presented the results of a retrospective investigation of the second biggest cohort of patients who had received MEG, SEEG, and surgery to date, with a longer follow-up than previous studies. In 42 patients who received MEG and SEEG surgery prior to resective epilepsy surgery, the researchers compared the MEG dipole mapping results with the SEEG

results and looked at their relationship with long-term seizure success. Three major findings emerged from this research: 1) Patients with concordant presurgical MEG and SEEG localization had a better surgical outcome than those with inconsistent localization; 2) patients with complete MEG cluster sampling had a better outcome than those with incomplete sampling; 3) MEG cluster results with specific features, such as a single cluster, tight clusters, and stable orientation, were associated with a better prognosis after SEEG implantation and resective surge.[2]

MEG data can help with SEEG electrode placement, and a completely sampled MEG anomalous area by SEEG predicts a better outcome after resective surgery. Patients who had the same SOZ location on MEG and SEEG had better outcomes. On MEG, a single, tight cluster or a steady orientation were similarly associated with improved outcomes following resective surgery.

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For the treatment of drug-resistant epilepsy in children, stereotactic laser interstitial thermal therapy corpus callosotomy was used.

For patients with diffuse or multifocal epileptic discharge resulting in generalised seizures, corpus callosotomy (CC) is a valuable palliative surgical option. The corpus callosum is thought to be the most essential pathway for the propagation of epileptic activity between the two hemispheres of the brain, according to the pathophysiologic foundation of CC.[1] MRgLITT (MR-guided laser interstitial thermal therapy) is a minimally invasive callosotomy alternative to open craniotomy. The aim of this study was to evaluate if MRgLITT callosotomy could be performed safely in paediatric patients with similar seizure control.[2]

This paper describes an institutional case series of 11 treatments for the treatment of drop attacks in drug-resistant primary generalised epilepsy patients in ten individuals. Complete callosotomy, anterior two-thirds, posterior, or ablation of remnant callosal fibres following earlier callosotomy were all done with MRgLITT (open or MRgLITT). The clinical course, operation details, radiographic imaging, clinical outcomes, and complications were all reviewed retrospectively.

The operation took between 4 and 8 hours, and the average hospital stay was two days. There were no issues to deal with. At the longest follow-up, 71 percent of the 7 patients with at least 3 months of follow-up achieved relief from drop attacks (Figure 3), and 57 percent of cases exhibited improvement in their other seizure semiologies as well (Engel Class II: 28 percent , Class III: 28 percent , Class IV: 43 percent).

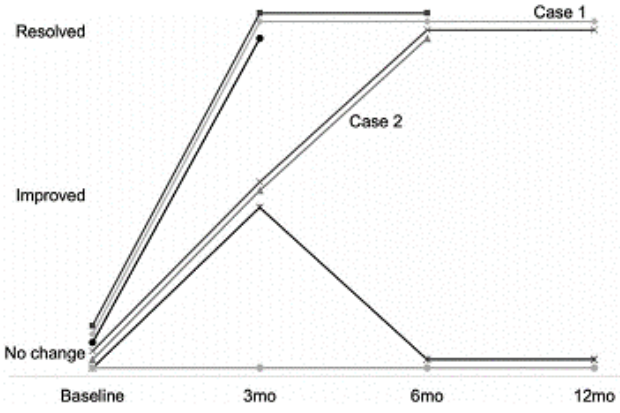

Figure 3: Timeline of postoperative changes in seizure frequency for the 7 patients with follow-up data.

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Table 2: Patient seizure outcomes

		Cases										
	Summary	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
Total follow-up (months)	8.6 ± 6.9	14.96	10.65	17.98	11.84	13.60	0.73	0.50	5.51	1.82	16.39	0.50
Atonic seizures												
Pre op seizures	7±6/d	10-15/d	1-3/d	NA	10-25/d	1-20/d	4-7/d	3-6/d	10	NA	1/d	1-3/d
Post-op seizures	4 ± 7 /wk	0	0	NA	0	0	0	3-6/d	0	NA	1/d	0-1/d
Other seizures												
Pre-op seizures	5 ± 9/d	20-30/d	1-3/day	1-2/ wk	5-8/d	1/d	3/wk	NA	1-5/d	1-100/d	2-3/mo	30/mo
Post-opseizures	1 ± 2/d	2-5/d	8-10/wk	1-2/ wk	2-3/d	0	0	NA	2-3/d	3-5/d	2-3/mo	0
Engel Class	70% improved	IV	II	IV	II	III	II	NA	III	III	IV	I

The researchers hypothesised that MRgLITT callosotomy could complement open callosotomy, with MRgLITT being the preferred treatment for medically difficult patients or those who had had previous surgery. After a failed open (or, in principle, MRgLITT) callosotomy, this approach can be used as a salvage treatment. The T1-weighted or FLAIR images used in the MRgLITT approach can be used to confirm the degree of ablation right away.[3] Even in individuals who had satisfactory clinical outcomes, postoperative imaging in this study revealed that there may have been modest amounts of remnant tissue in the corpus callosum. While the surviving fibres may be easily visible, others may become more visible after three months. It's unknown if this tissue is made up of functioning fibres or gliotic tissue, thus more research is needed to figure out what role this leftover tissue plays in seizure independence. Similar findings have been found by others, including Huang et al. If clinically indicated, repeat MRgLITT ablation may be done to ablate residual fibres.[2,4]

In the care of juvenile patients with medically intractable epilepsy characterised by drop attacks, MR-guided LITT callosotomy is a safe and successful method. While this is one of the largest paediatric studies to date, more research is needed to determine its safety and efficacy in these individuals.

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A case report of successful medical therapy of West syndrome with a KCNA2 mutation.

Epileptic spasms that occur in clusters and significant interictal epileptiform discharges characterise West syndrome, an age-related epileptic condition that affects children from infancy and early childhood. The substantial risk of cognitive decline in children with West syndrome necessitates early and intensive anti-epileptic medication.[1] There hasn't been any evidence that KCNA2 gene variant causes West syndrome. The clinical and behavioural characteristics of West syndrome induced by the c.244C>T (p.Arg82Cys) pathogenic mutation of KCNA2 are highlighted in this report for the first time. This research contributes to our knowledge of the genetic and phenotypic spectrum of KCNA2-related West syndrome.[2]

Case Presentation:

Based on the clinical manifestations and EEG results, a 4-month-old boy with epileptic spasms was diagnosed with West syndrome. Three whole-exome sequencing (WES) tests were done, as well as protein structure model prediction. A literature search was used to investigate the clinical and genetic aspects of this disease, as well as the mechanisms of action of topiramate (TPM). The link between TPM's effect and the pathophysiology of the KCNA2 mutation was also investigated. In this patient, the WES test revealed a c.244C>T/p. Arg82Cys variant of KCNA2 (NM 004974.3), which was identified as a de novo mutation by Sanger sequencing. This is the first report of the c.244C>T/p. Arg82Cys variant in KCNA2, which was likely a harmful mutation, as far as we know. After sodium valproate, massive doses of vitamin B6, and adrenocorticotropic hormone failed, TPM successfully controlled seizures for ten months (Figure 4 & 5). TPM's therapeutic effect in this patient is thought to be attributable in part to the suppression of carbonic anhydrase, according to the study.

The case was described as having generalised seizures that manifested as epileptic spasms and frequent seizures, and was identified as early-onset West syndrome in this report. With sodium valproate, substantial doses of vitamin B6, and adrenocorticotropic hormone, the condition proved difficult to treat. Interictal EEG showed hypsarrhythmia and multifocal epileptiform discharges, especially in the bilateral posterior areas, and burst suppression, comparable to the described GOF effect on EEG discharges. These aberrant EEG recordings were also accompanied by psychomotor impairment and cerebellar involvement, but no evident ataxia. As a result, this case was diagnosed as KCNA2 GOF mutation-related encephalopathy, which has a severe phenotype.[2] Gong P et colleagues found that KCNA2 gene variations can cause developmental and epileptic encephalopathy, as well as a variety of seizures. The most prevalent is loss-of-function c.1214C>T, which causes seizures to begin in childhood with Rolandic discharges that tend to develop into the ESES pattern. The c.1120A>G mutation is both a gain-of-function and a loss-of-function variant; individuals with c.1120A>G experience

seizures that begin in the newborn period; the phenotype overlaps with the former but is more severe.[3]

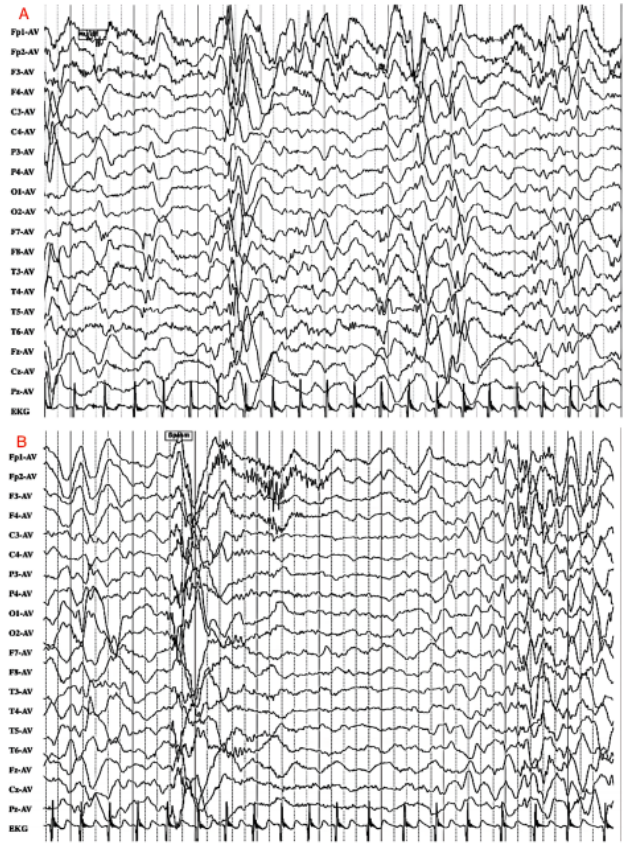

Figure 4: Abnormal EEG at age of 6months (on June 20, 2019). The background activity was completely disorganized and chaotic on interictal EEG, showing hypsarrhythmia. When the patient was awake, the susceptible ictal EEG showed fexor spasms

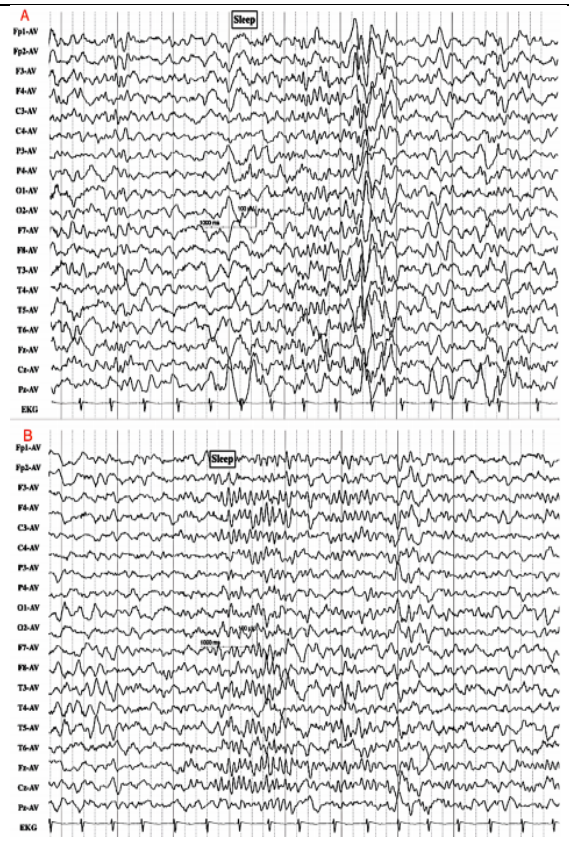

Figure 5: EEG at age 1 year and 3months (on March 19, 2020). After almost 8months of TPM treatment, EEG showed low-amplitude fast waves when he was awake or sleeping

Patients with West syndrome should be tested for mutations in the KCNA2 gene. For KCNA2-related diseases, the TPM therapy is likely to be effective.

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